II. REMARKS

Preliminary Remarks

The request for continued examination filed November 15, 2007 has been entered and the finality of the previous official action has been withdrawn. Claims 38, 39, 42, 44-51, 56-63, 65, 67-70, 72-75, 78-80, 83, 84, 86-92, 94-100, 102-105, 107, 108, 110-116, 118, 119, 121-123, and 126-141 were examined. Claims 38 and 51 are currently amended. Upon entry of the amendment, claims 38, 39, 42, 44-51, 56-63, 65, 67-70, 72-75, 78-80, 83, 84, 86-92, 94-100, 102-105, 107, 108, 110-116, 118, 119, 121-123, and 126-141 will be pending in this application.

Independent claims 38 and 51 are amended to specify that the methods of the claimed invention consist essentially of the recited steps. Also, claims 38 and 51 are amended to specify that the dose of exogenous LH and FSH or HMG remains the same throughout the treatment period. This is supported by the application as originally filed, including at pages 8-9 and Table II.

The applicant does not intend by these or any amendments to abandon subject matter of the claims as originally filed or later presented, and reserves the right to pursue such subject matter in continuing and/or divisional applications.

Reconsideration and allowance of the present application based on the above-described amendments and the following remarks are respectfully requested.

Patentability Remarks

35 U.S.C. §102(b)

Diedrich *et al.*

Claims 38, 39, 42, 44-46, 48-51, 56-58 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Diedrich *et al.* (Hum Reprod. 1994). Diedrich *et al.* describe a method for obtaining the production of a fertilizable oocyte within a program of COS/ART comprising (a) administering HMG to induce follicle growth, and (b) administering cetrorelix in a dosage regimen of multiple daily doses of 3 mg/day to prevent a premature LH surge, wherein the first

daily dose of cetrorelix was administered on day 7 of the cycle, and daily treatment continued until ovulation was induced by administration of HCG when the leading follicle reached a diameter of 18-20 mm and plasma estradiol levels were > 300 pg/ml per follicle of ≥ 15 mm in diameter. Diedrich *et al.* also describe performing the same method wherein cetrorelix is administered in a dosage regimen of multiple daily doses of 1 mg/day. *See* page 788, left column, and page 789, paragraph 2 of Materials and methods. As shown in Figures 1 and 2 on page 789, daily doses of cetrorelix were administered from day 7 until ovulation was induced on day 14 or day 15 of the cycle.

The applicants respectfully submit that the claims of the present application are directed to a method that is different from and is not anticipated by the method described by Diedrich *et al.*

To anticipate a claim, a reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Citations omitted; *see* above, and Manual for Patent Examining Procedure (M.P.E.P.), §2131.

Pending claims 38, 39, 42, 44-46, 48-51, 56-58 and 60 are not anticipated by Diedrich *et al.*

Independent claims 38 and 51 are amended to specify that the methods of the claimed invention consist essentially of the recited steps. Claims 38 and 51 are directed to a method for obtaining the production of a fertilizable oocyte within a program of COS/ART comprising (a) administering LH and FSH to induce follicle growth, and (b) administering an LHRH antagonist in a single or dual dosage regimen of 3 mg per dose, beginning on cycle day 1 to 10, to prevent a premature LH surge, wherein the dosage regimen is selected to suppress endogenous LH secretion, but does not suppress endogenous FSH secretion, which is maintained at a natural level.

Diedrich *et al.* describe a method wherein cetrorelix is administered in a dosage regimen of multiple daily doses of 3 mg/day starting on day 7 of the cycle and continuing until ovulation was induced on about day 14 or day 15 of the cycle, in order to prevent a premature LH surge, as discussed above. Diedrich *et al.* do not describe a method comprising administering an LHRH

antagonist in a single or dual dosage regimen of 3 mg per dose to prevent a premature LH surge with no effect on FSH levels. The examiner states that the use of comprising language allows for additional steps in the method not specified in the claims, and therefore, the claims are not limited to a single or dual dose of 3 mg of the LHRH antagonist. Official action at page 3. Also, the examiner states that the arguments relating to the effect on endogenous FSH levels has been considered, but are not persuasive. Official action at pages 3-4. Specifically, the examiner asserts that because the claims encompass the method steps of Deidrich *et al.*, and because the art cited by the applicants and post-filing date art do not provide sufficient evidence that the two methods can be distinguished, the arguments are not persuasive. Official action at page 4. The examiner is mistaken regarding the art cited and the arguments presented.

As stated above, claims 38 and 51 set forth a method wherein the dosage regimen of the LHRH antagonist is selected so that endogenous LH levels are suppressed, but endogenous FSH levels are not. Also, as stated previously, the methods taught by Deidrich *et al.*, 3mg/day, or 1mg/day starting on day 7 and continuing until ovulation, result in suppression of LH levels and FSH levels. Deidrich *et al.*, states, "[t]he suppression of FSH under Cetrorelix treatment was less pronounced, but this might have been due to the longer plasma half-life of the injected FSH." Deidrich *et al.*, at page 790, left column. Deidrich *et al.*, therefore, states that <u>there was suppression of FSH levels</u>, but that it was not as pronounced as it could have been due to the longer plasma half-life of the FSH that was administered to the patient. The examiner admits as much in the official action by stating in discussing the Albano *et al.* reference cited by the applicants that "unlike that of Deidrich *et al.*, administration of Cetrorelix did not result in a decrease in FSH levels." Official action at page 4.

Regarding Albano *et al.*, "Hormonal profile during the follicular phase in cycles stimulated with a combination of human menopausal gonadotrophin-releasing hormone antagonist (Cetrorelix)," Human Reproduction, Vol. 11, No. 10, pp. 2214-18 (1996), which teaches a method of administering 0.5mg/day of Cetrorelix starting on day 6, the examiner is mistaken regarding the applicants arguments in relation to this reference. The applicants cited this article to demonstrate that those of skill in the art that had reviewed the Deidrich *et al.*, reference had determined that the method taught by Deidrich *et al.*, resulted in a decrease in FSH

levels. This is evident from the applicants citation to the disclosure of Albano *et al.*, that, "[i]n contrast with other studies, where plasma FSH concentration slightly decreased simultaneously with LH concentration (Deidrich *et al.*, 1994; Olivennes *et al.*, 1994), our study did not reveal a decrease in FSH after the administration of the antagonist (Figure 1)." Albano *et al.*, at page 2116, right column. Additionally, the examiner misplaces emphasis on the disclosure in Albano *et al.*, that the maintenance of FSH levels may be associated with the lower dose of antagonist used or possibly to the influence of the exogenous FSH used and alleges that the art cited does not distinguish between added and endogenous FSH levels. The applicants draw the examiner's attention to the differences between the Deidrich *et al.*, and Albano *et al.*, references. The dose of antagonist used in Albano *et al.*, is approximately one sixth of the dose used by Deidrich *et al.*, while both references use exogenous FSH. Deidrich *et al.*, show a decrease in FSH levels, whereas Albano *et al.*, allege that there is no decrease in FSH levels. As both references use exogenous FSH, any difference in FSH levels observed must be due to endogenous FSH levels. The art cited, therefore, does distinguish between endogenous and exogenous FSH levels, although it does not expressly state this.

One of skill in the art at the time of the Albano *et al.* reference, therefore, was aware and understood that the methods taught by Deidrich *et al.* cause a suppression of both LH and FSH. Currently amended claims 38 and 51 encompass a method wherein the endogenous LH level is suppressed, but FSH is not. The methods taught by Deidrich *et al.*, therefore, do not teach every element as set forth in the claim, either expressly or inherently. Accordingly, claims 38 and 51, and pending claims 39, 42, 44-46, 48-50, 56-58 and 60 that depend on claims 38 and 51, are not anticipated by Diedrich *et al.* under 35 U.S.C. §102(b).

In view of the foregoing, withdrawal of the rejection of claims 38, 39, 42, 44-46, 48-51, 56-58 and 60 under 35 U.S.C. §102(b) as allegedly being anticipated by Diedrich *et al.* is respectfully requested.

35 U.S.C. §102(a)

Olivennes *et al.*

Claims 38, 39, 42, 44-46, 48-51, 56-58 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Olivennes *et al.*, "Scheduled administration of a gonadotrophin-releasing hormone antagonist (Cetrorelix) on day 8 of in-vitro fertilization cycles: a pilot study," Human Reprod., 10:1382-86 (1995). Specifically, the examiner alleges that Olivennes *et al.*, teach the use of a single or dual dose of 3 mg of Cetrorelix on day 8 of the menstrual cycle, with administration of an exogenous gonadotrophin to induce follicle growth, ovulation occurring between day 9 and day 20 of menstrual cycle, and a decrease in LH levels but no change in FSH levels. Official action at page 5.

Olivennes *et al.*, disclose a method of administering 3 mg of Cetrorelix on day 8 of the menstrual cycle, with administration of an exogenous gonadotrophin to induce follicle growth, ovulation occurring between day 9 and day 20 of menstrual cycle, and a decrease in LH levels but no change in FSH levels. Olivennes *et al.*, however, disclose that the dose of human menopausal gonadotrophin was increased on the day the Cetrorelix was administered and that this may have contributed to the normal oestradiol plasma concentration observed. Olivennes *et al.*, at 1383, left column and 1385 right column. As noted above, claims 38 and 51 are amended to encompass methods wherein the dose of HMG (or the combination of LH and FSH in claim 38) is not changed during the treatment period. Olivennes *et al.*, because it teaches an increase in HMG dose on the day of administering the Cetrorelix, therefore, does not teach each and every element of the claims. Accordingly, claims 38 and 51, and pending claims 39, 42, 44-46, 48-50, 56-58 and 60 that depend on claims 38 and 51, are not anticipated by Olivennes *et al.* under 35 U.S.C. §102(a).

In view of the foregoing, withdrawal of the rejection of claims 38, 39, 42, 44-46, 48-51, 56-58 and 60 under 35 U.S.C. §102(a) as allegedly being anticipated by Olivennes *et al.* is respectfully requested.

Obvious-Type Double Patenting Rejection

Claims 38-39, 42, 45-51, 56-62, 65, 67-74, 78-82, 86-92, 94-100, 102-105, 107-108, 110-116, 118-119, 121-123, 126-128 and 129-141 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22, 26-42 of co-pending U.S. Application No. 10/661,780. The claims of Application No. 10/661,780 are directed to a method of treating infertility disorders that comprises inducing follicle growth by administration of hMG or recombinant FSH in combination with clomiphene, which method is considered to be encompassed by the claims of the present application. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The examiner states that because the provisional double patenting rejection is not the only grounds for rejection, it must be maintained, despite the applicants arguments presented in the November 15, 2007 response. The applicants acknowledge that the examiner has maintained the rejection and restate their request that following withdrawal of the other basis for rejection, which the applicants submit have been overcome with this response, that the examiner withdraw the rejection based on nonstatutory obviousness-type double patenting and permit the application to issue as a patent without a terminal disclaimer, pursuant to M.P.E.P. § 804 I.B.1.

III. CONCLUSION

In view of the foregoing, the applicants believe that the claims are in form for allowance, and hereby respectfully solicit such action. If any point remains in issue which the examiner feels may be best resolved through a personal or telephone interview, the examiner is strongly urged to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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